

AD-A095 572

AIR FORCE OCCUPATIONAL AND ENVIRONMENTAL HEALTH LAB --ETC F/S 6/20
THE EFFECTS OF SCAVENGING ON WASTE METHOXYFLURANE CONCENTRATION--ETC(U)
JAN 81 J E MILLIGAN, J L SABLAN, J F CROY

UNCLASSIFIED OEHL-TP-81-1

NL

1 of 1
ADA
W88-112

END
DATE
FILMED
3-81
DTIC

LEVEL II

10

Report OEHL TP-81-1
USAF OEHL TECHNICAL REPORT



USAF OEHL TECHNICAL REPRINT

AD A095572

The Effects of Scavenging on Waste Methoxyflurane
Concentrations in Veterinary Operating Room Air

Approved for public release; distribution unlimited

REC 27 1981

A

USAF Occupational and Environmental Health Laboratory
Aerospace Medical Division (AFSC)
Brooks Air Force Base, Texas 78235

81 2 27 042

NOTICES

When US Government drawings, specifications, or other data are used for any purpose other than a definitely related Government procurement operation, the Government thereby incurs no responsibility nor any obligation whatsoever, and the fact that the Government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data, is not to be regarded by implication or otherwise, as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

The mention of trade names or commercial products in this publication is for illustration purposes and does not constitute endorsement or recommendation for use by the United States Air Force.

Do not return this copy. Retain or destroy.

Please do not request copies of this report from the USAF Occupational and Environmental Health Laboratory. Additional copies may be purchased from:

National Technical Information Service
5285 Port Royal Road
Springfield, Virginia 22161

Federal Government Agencies and their contractors registered with the (DDC) should direct requests for copies of this report to:

Defense Technical Information Center (DTIC)
Cameron Station
Alexandria, Virginia 22314

This report has been reviewed by the Public Affairs Office and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

William E. Mabson
WILLIAM E. MABSON, Colonel, USAF, BSC
Commander

30 OCT 1951

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

416 936

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

well documented. There are, however, few reports of the potential hazard to veterinary personnel. The present study was conducted to determine the exposure levels to methoxyflurane in a veterinary surgery. Real-time analyses were obtained utilizing infrared spectrophotometry. Measurements were made both during scavenging and not scavenging of the waste anesthetic gas. The mean level of methoxyflurane during scavenging was significantly different from the mean during not scavenging. Furthermore, the 95 percent upper confidence limit for the scavenged mean was within the two parts per million standard for methoxyflurane recommended by the National Institute for Occupational Safety and Health. The 95 percent upper confidence limit for the not scavenged mean was well above that standard. Protection of veterinary personnel and animal researchers from chronic exposure to methoxyflurane vapors, therefore, seems advisable and achievable. Complete waste anesthetic gas management and periodic monitoring programs should be established to protect personnel involved.

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

TABLE OF CONTENTS

	Page
PREFACE	ii
INTRODUCTION	1
MATERIALS AND METHODS	4
RESULTS	6
DISCUSSION	9
CONCLUSIONS	11
ACKNOWLEDGEMENTS	12
LITERATURE CITED	13

PREFACE

This article was originally printed in: "Trace Substances In Environmental Health-XIV", D.D. Hemphill, ed., Univ. Missouri, 1980.

It was edited for reprint as a USAF OEHL Technical Reprint by Lt Col Joseph E. Milligan, with permission from the original publisher.

This article represents the first documentation of methoxyflurane levels in veterinary surgeries under controlled conditions, and the effects of scavenging on those waste gas levels.

INTRODUCTION

We live in an age of increasing awareness and concern about occupational health and diseases associated with environmental pollution. Attention has been called to the possible adverse effects of trace anesthetic gases in human surgeries (12). Veterinarians, their assistants, and animal researchers who use gaseous anesthetics on a regular basis should also consider the potential environmental hazards posed by these chemicals.

Interest in trace anesthetic gases was stimulated in 1967 by a survey of 303 Russian anesthesiologists who reported a high incidence of nausea, irritability, headache, fatigue and pruritus, and an alarming rate of spontaneous abortions (32). Subsequent to this report, a number of human epidemiologic studies, and laboratory animal experiments have been conducted in an attempt to identify any prominent health effects associated with chronic exposure to waste anesthetic gases.

The major adverse human health effects identified by the epidemiologic surveys were abortion and congenital abnormalities. An increased incidence of spontaneous abortion in exposed female workers (1, 6, 7, 8, 14, 18, 19) and of congenital abnormalities among their children (9, 10, 11, 18, 19) were found. The same increases among the unexposed wives and children of exposed men were also noticed (1, 7, 8, 19). These human epidemiologic surveys, furthermore, described effects on fertility (18), hepatic and renal diseases (9, 10, 31), the central nervous system (31, 32) and the risk of cancer (3, 7, 11) following exposure to anesthetic gases.

Experimental evidence from laboratory animal studies is supportive of the suggestion that health hazards are actually caused by methoxyflurane exposure. Higher embryonic death rates and an increased percentage of fetal anomalies

have occurred following exposure of chick eggs to methoxyflurane (28). High subanesthetic concentrations of methoxyflurane have also caused fetal growth retardation in rats (25). Hepatomegaly and histologic changes of the liver have been demonstrated in rats following chronic exposure to low concentrations of methoxyflurane (5). Furthermore, methoxyflurane has been found to alter the immune response in mice (15), and it has been suggested that interference with immune mechanisms by anesthetics would be expected to influence the course of tumor development (4). Still another potentially hazardous effect of methoxyflurane is enzyme induction. Enzyme induction by subanesthetic doses of methoxyflurane has been demonstrated in the rat (2).

Concentrations of methoxyflurane in human operating rooms have been reported to be 1.3-9.8 parts per million (ppm) around the anesthetist and 1.0-2.0 ppm around the surgeon (9). However, is breathing trace amounts of methoxyflurane in veterinary and animal research facilities a personal or personnel hazard? The evidence for or against is scanty. There have been few scientifically documented reports of measurements of methoxyflurane in veterinary surgeries. An uncontrolled survey of small animal veterinary hospitals reported methoxyflurane concentrations of 1.0-2.6 ppm at the breathing zone of the veterinary surgeon, and 1.3-3.2 ppm at the breathing zone of the animal technician (26). Another report shows the methoxyflurane concentration in a small animal surgery to be 6.9 ppm (34).

Until the present, therefore, we have looked only at data gathered in human surgeries, along with a few limited surveys conducted in veterinary surgeries, and concluded that efforts should be made to depollute veterinary and animal research preparation, operating and recovery rooms. Consequently, the following study of methoxyflurane concentrations in the operating room air

of a veterinary surgery was conducted under controlled conditions. The primary emphasis of this study was to establish analytically determined values of exposure concentrations of methoxyflurane at the breathing zone of veterinary personnel, both during scavenging and not scavenging of the waste anesthetic gas.

MATERIALS AND METHODS

Twelve dogs, ranging in weight from 17.7-23.0 kg, were anesthetized for two hours each. The dogs were initially anesthetized with an injectable anesthetic, with maintenance anesthesia produced through inhalational techniques as described by Short (27). Methoxyflurane was delivered via a semi-closed system using Copper Kettle and Vernitrol vaporizers. Gas flow rates and vaporizer settings were: 3ℓ/min O₂; 0.5% methoxyflurane. The dogs' ventilatory patterns were assisted by intermediate positive pressure breathing. The anesthetist judged the depth of anesthesia by monitoring an electrocardiogram.

Methoxyflurane concentrations in the operating room air were determined directly by infrared spectrophotometry using a Wilks Miran-1A General Purpose Gas Analyzer (Wilks/Foxboro Analytical, Norwalk, CT). The sampling parameters using the infrared spectrophotometer were: wavelength, 9.1 μm; slit setting, 1.0 mm; absorbance range, 0-0.25 units; pathlength, 14.25 m; volume, 5.6 ℓ; windows, Na Cl. Calibration of the infrared spectrophotometer, construction of standard curves and calculations were based on the operation, maintenance and service manual for the instrument (24).

The 12 dogs were randomly placed into two groups. One group of six dogs was anesthetized while practicing waste anesthetic gas scavenging techniques, as described by Whitcher and Rock (35), and Manley and McDonell (20). The other group of six dogs was anesthetized without the employment of a waste anesthetic gas scavenging system. Methoxyflurane measurements were taken at four time intervals (4, 36, 68, 100 minutes after the start of the procedure) and at the following four locations in the operating room: breathing zone, anesthetist; breathing zone, surgeon; breathing zone, dog; and at the operating room exhaust vent. The data collected were statistically evaluated by analysis

of variance, and the 95 percent upper confidence limit was determined for each group mean (29).

RESULTS

The data collected in this study are shown in Table I. Results of the statistical analyses are summarized in Table II. The range of methoxyflurane concentrations in 96 air samples measured during scavenging was 0-1.25 ppm, while the range of 96 measurements during not scavenging was 0.25-75.00 ppm. The mean methoxyflurane concentration during scavenging (0.58 ppm) was significantly different ($p < .05$) from the mean during not scavenging (4.75 ppm). Furthermore, the 95 percent upper confidence limit for the mean of the scavenged group (0.91 ppm) was within the National Institute for Occupational Safety and Health (NIOSH) recommended standard for methoxyflurane of 2 ppm (13). However, the 95 percent upper confidence limit for the mean of the not scavenged group (17.24 ppm) was well above that NIOSH recommended standard. There was no significant difference in methoxyflurane concentrations due to time of measurement. There was, however, a significant difference between the overall position means ($p < .05$), as well as a group X position interaction ($p < .05$). The highest mean concentration of methoxyflurane during not scavenging (12.08 ppm) was at the breathing zone, dog (D). In terms of personnel exposure during not scavenging, the surgeon (S) was exposed to a mean of 4.05 ppm methoxyflurane, while the anesthetist (A) was exposed to a mean of 1.36 ppm methoxyflurane. The mean methoxyflurane concentration at the exhaust vent (V) during not scavenging was 1.53 ppm. There was no significant difference between the position means of the scavenged group (D, 0.63 ppm; S, 0.61 ppm; A, 0.52 ppm; V, 0.57 ppm). There were no group X time, position X time, or group X position X time interactions.

TABLE I. METHOXYFLURANE CONCENTRATIONS (ppm) IN VETERINARY OPERATING ROOM AIR DURING SCAVENGING AND NOT SCAVENGING

Group	Scavenged				Not Scavenged			
	4	36	68	100	4	36	68	100
Time after start of procedure, min								
Position ^{a,b}								
D	.43±.09	.55±.06	.70±.05	.84±.11	21.95±13.22	9.31±6.24	14.82±12.05	2.23±.30
A	.40±.09	.44±.06	.53±.05	.74±.11	.66±.13	1.33±.12	1.60±.11	1.85±.10
S	.43±.12	.58±.08	.61±.07	.80±.10	10.17±5.79	2.19±.54	2.02±.21	1.82±.13
V	.49±.10	.49±.07	.59±.06	.68±.05	.98±.11	1.60±.10	1.68±.13	1.87±.09

^aBreathing zone, dog (D); breathing zone, anesthetist (A); breathing zone, surgeon (S); exhaust vent (V)

^bEach value is the mean of six observations, ± standard error of the mean

TABLE II. GROUP AND POSITION MEANS OF METHOXYFLURANE CONCENTRATIONS (ppm) IN VETERINARY OPERATING ROOM AIR

Group	Scavenged	Not Scavenged
Position mean ^{a,b}		
D	0.63±.05	12.08±4.67 ^c
A	0.52±.01	1.36±0.11 ^d
S	0.61±.05	4.05±1.54 ^e
V	0.57±.04	1.53±0.09 ^f
Group mean ^{g,h}	0.58±.01	4.75±1.29
95% upper confidence limit of the group mean	0.91	17.24

^aBreathing zone, dog (D); breathing zone, anesthetist (A); breathing zone, surgeon (S); exhaust vent (V)

^bEach value is the mean of 24 observations, ± standard error of the mean, and averaged across four time intervals with no interactions

^{c,d,e,f}Means having different superscripts in the same column are significantly different ($p < .05$)

^gEach value is the mean of 96 observations, ± standard error of the mean, and averaged across four positions and four time intervals. There was a group X position interaction ($p < .05$). There were no group X time, position X time, or group X position X time interactions

^hGroup means are significantly different ($p < .05$)

DISCUSSION

Evidence that occupational exposure to methoxyflurane constitutes a health hazard is circumstantial, being based on human epidemiologic surveys and laboratory animal studies. A cause and effect relationship in humans has not been documented. Other factors affecting medical personnel, such as stress, fatigue, and unfavorable working hours may be involved. Nevertheless, the potential harm of the long-term exposure to methoxyflurane should not be ignored. Methoxyflurane has been detected in end-expired air of anesthesiologists for as long as 30 hours after exposure (9). Furthermore, methoxyflurane is not an inert compound, and as much as 50 percent may be metabolized (17). Biotransformation of methoxyflurane, unlike many drugs, does not result in reduced toxicity since its metabolites are hepatotoxic (30) and nephrotoxic (22, 23, 30). An increased concentration of fluoride ion, a nephrotoxic methoxyflurane metabolite, has been found in an anesthesiologist following 6 1/2 hours of occupational exposure to methoxyflurane (9). The high fat-solubility of methoxyflurane, therefore, results in availability of a depot of drug for prolonged postexposure biotransformation (17) and possible long-term susceptibility to the toxic effects of methoxyflurane and its metabolites (9).

To insure personnel safety, NIOSH has recommended in its Criteria Document on Waste Anesthetic Gases and Vapors (12) that a concentration level of 2 ppm should not be exceeded for methoxyflurane. The results of this experiment show, decisively, that veterinary and animal research personnel are subjected to concentrations of methoxyflurane in excess of the standard recommended by NIOSH. However, since there are some indications that the toxic effects of methoxyflurane are dose related (16, 21), and since the lag time between exposure and disease may be as long as 20 years (36), there may be no safe

level of exposure to methoxyflurane. It, therefore, seems prudent to limit personnel exposure to methoxyflurane to as low a concentration as possible.

It has been shown that dilution ventilation, alone, has no significant effect on reducing waste methoxyflurane concentrations in veterinary surgeries (26). However, one study demonstrated a tenfold reduction in anesthetic gas concentrations in human operating rooms with scavenging (33), while another study achieved a 50 percent reduction of methoxyflurane concentrations in human delivery rooms using a scavenging apparatus (13). Two limited surveys have indicated the potential ability of scavenging techniques to depollute veterinary operating room air. In a small animal survey using a semi-closed anesthetic system, scavenging reduced methoxyflurane concentrations to 0.3-0.4 ppm (26). In another small animal surgery, a dramatic reduction of the methoxyflurane concentration was also achieved when scavenging was instituted (34). The results of this study confirm these reports and clearly demonstrate the effectiveness of anesthetic gas scavenging techniques in reducing methoxyflurane concentrations in veterinary surgeries.

The highest methoxyflurane concentrations were detected at the dogs' breathing zone. These high readings were probably due to an incomplete seal around the endotracheal tube. The group X position interaction, therefore, demonstrates the efficacy of scavenging in eliminating this particular leak hazard.

CONCLUSIONS

Without waste anesthetic gas scavenging, methoxyflurane concentrations in veterinary surgeries are well above the NIOSH recommended standard of 2 ppm. With waste anesthetic gas scavenging, methoxyflurane concentrations in veterinary surgeries are within the NIOSH recommended standard of 2 ppm. Protection of veterinary personnel and animal researchers from chronic exposure to methoxyflurane vapors, therefore, seems both advisable and achievable. Complete waste anesthetic gas management and periodic monitoring programs should be established to protect personnel involved.

ACKNOWLEDGEMENTS

The authors would like to express appreciation to C.E. Short, Professor and Chief, Anesthesiology, NYSCVM, Cornell University, for his expert advice. We are also grateful to J.C. Rock, P. Swerzenski, and C.E. Thalken for their consultative and technical assistance.

LITERATURE CITED

1. Askrog, V. and B. Harvald. 1970. Teratogenic effect of inhalation anesthetics. Nord. Med. 833:498-504.
2. Berman, M.L. and J.F. Bochantin. 1970. Nonspecific stimulation of drug metabolism in rats by methoxyflurane. Anesthesiology 32:500-506.
3. Bruce, D.L., K.A. Eide, H.W. Linde and J.E. Eckenhoff. 1968. Causes of death among anesthesiologists. A 20-year study. Anesthesiology 29:565-569.
4. Bruce, D.L. and D.W. Wingard. 1971. Anesthesia and the immune response. Review article. Anesthesiology 34:271-282.
5. Chenoweth, M.B., B.K.J. Leong, G.L. Sparschu and T.R. Torkelson. 1972. Toxicities of methoxyflurane, halothane and diethyl ether in laboratory animals on repeated inhalation of subanesthetic concentrations. In: Cellular Biology and Toxicity of Anesthetics, B.R. Fink, Ed., Williams and Wilkins Co., Baltimore, pp. 275-285.
6. Cohen, E.N., J.W. Belvill and B.W. Brown, Jr. 1971. Anesthesia, pregnancy, and miscarriage: A study of operating room nurses and anesthesiologists. Anesthesiology 35:343-347.
7. Cohen, E.N., B.W. Brown, D.L. Bruce, H.F. Cascorbi, W. Corbett, J.H. Jones and C.E. Whitcher. 1974. Occupational disease among operating room personnel: A national study. Anesthesiology 41:321-340.
8. Cohen, E.N., B.W. Brown, D.L. Bruce, H.F. Cascorbi, W. Corbett, J.H. Jones and C.E. Whitcher. 1975. A survey of anesthetic health hazards among dentists. J. Am. Dent. Assoc. 90:1291-1296.
9. Corbett, T.H. and G.L. Ball. 1971. Chronic exposure to methoxyflurane: A possible occupational hazard to anesthesiologists. Anesthesiology 34:532-537.

10. Corbett, T.H., R.G. Cornell, J.L. Endres and K. Lieding. 1974. Birth defects among children of nurse - anesthetists. *Anesthesiology* 41:341-344.
11. Corbett, T.H., R.G. Cornell, K. Lieding and J.L. Endres. 1973. Incidence of cancer among Michigan nurse - anesthetists. *Anesthesiology* 38:260-263.
12. Criteria for a Recommended Standard - Occupational Exposure to Waste Anesthetic Gases and Vapors. 1977. HEW Publication No. (NIOSH) 77-140. US Dept. of Health, Education and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, 194 pp.
13. Dahlgren, B-E., L. Olander and P. Ovrum. 1979. Pollution of delivery ward air by nitrous oxide-methoxyflurane. *Am. Ind. Hyg. Assoc. J.* 40:666-672.
14. Garstka, K., K.L. Wagner and M. Hamacher. 1974. Pregnancy complications in anesthesiologists. *Proc. 159th Meeting, Lower Rhine-Westphalia Gyn. Obs. Assoc., The Women's Clinic, Bonn University, Bonn, West Germany.*
15. Goldstein, E., E.S. Munson, C. Eagle, R.W. Martucci and P.D. Hoeprich. 1971. The effects of anesthetic agents on murine pulmonary bactericidal activity. *Anesthesiology* 34:344-352.
16. Goto, Y., C.A. Dujovne, D.W. Shoeman and K. Arakawa. 1976. Liver Cell Culture Toxicity of General Anesthetics. *Toxicol. Appl. Pharmacol.* 36:121-130.
17. Holaday, D.A., S. Rudofsky and P.S. Treuhaft. 1970. The metabolic degradation of methoxyflurane in man. *Anesthesiology* 33:579-593.
18. Knill-Jones, R.P., D.D. Moir, L.V. Rodriques and A.A. Spence. 1972. Anesthetic practice and pregnancy: Controlled survey of women anesthetists in the United Kingdom. *Lancet* 1:1326-1328.

19. Knill-Jones, R.P., B.J. Newman and A.A. Spence. 1975. Anesthetic practice and pregnancy: Controlled survey of male anesthetists in the United Kingdom. *Lancet* 2:807-809.
20. Manley, S.V. and W.N. McDonell. 1980. Recommendations for reduction of anesthetic gas pollution. *J.A.V.M.A.* 176:519-524.
21. Mazze, R.I. 1971. Renal toxicity of anesthetics. A.S.A. refresher course lectures, 116A.
22. Mazze, R.I., M.J. Cousins and J.C. Kosek. 1972. Dose-related methoxyflurane nephrotoxicity in rats: A biochemical and pathological correlation. *Anesthesiology* 36:571-587.
23. Mazze, R.I., J.R. Trudell and M.J. Cousins. 1971. Methoxyflurane metabolism and renal dysfunction: Clinical correlation in man. *Anesthesiology* 35:247-252.
24. Miran-IA Infrared Gas Analyzer: Operation, Maintenance and Service Manual. 1978. Wilks, Norwalk CT, 88 pp.
25. Pope, W.D.B., M.J. Halsey, D. Phil, A.B.G. Lansdown, A. Simmonds and P.E. Bateman. 1978. Fetotoxicity in rats following chronic exposure to halothane, nitrous oxide, or methoxyflurane. *Anesthesiology* 48:11-16.
26. Ruby, D.L., R.M. Buchan and B.J. Gunter. 1980. Waste anesthetic gas and vapor exposures in veterinary hospitals and clinics. *Am. Ind. Hyg. Assoc. J.* 41:229-231.
27. Short, C.E. 1974. Clinical Veterinary Anesthesia: A Guide for the Practitioner, The C.V. Mosby Co., St. Louis, 231 pp.
28. Smith, B.E., M.L. Graub and F. Moya. 1965. Investigations into the teratogenic effects of anesthetic agents: The fluorinated agents. *Anesthesiology* 26:260-261.

29. Steel, R.G.D. and J.H. Torrie. 1960. Principles and Procedures of Statistics, McGraw-Hill Book Co., New York, 481 pp.
30. Torkelson, T.R., C.D. Kary, M.B. Chenoweth and E.R. Larsen. 1971. Single exposure of rats to the vapors of trace substances in methoxyflurane. *Toxicol. Appl. Pharmacol.* 19:1-9.
31. Uhlirva, A. and J. Polorny. 1974. Results of questionnaire survey of health damage to anesthesiologists. *Rozhl. Chir.* 53:761-770.
32. Vaisman, A.I. 1967. Working conditions in surgery and their effect on the health of anesthesiologists. *Eksp. Khir. Anesteziol.* 3:44-49.
33. Whitcher, C.E., E.N. Cohen and J.R. Trudell. 1971. Chronic exposure to anesthetic gases in the operating room. *Anesthesiology* 35:348-353.
34. Whitcher, C.E. and R. Hart. 1979. Unpublished data, US Dept. of Health, Education and Welfare (NIOSH).
35. Whitcher, C.E. and J.C. Rock. 1978. Control of occupational exposure to inhalational anesthetics - current status. OEHL Report TP-78-1, USAF Occupational and Environmental Health Laboratory, Aerospace Medical Division, Brooks AFB TX, 21 pp.
36. White, R.J. 1978. Pollution control in the operating room. *Vet. Clinics N. Amer.* 8:337-342.

DATE
FILMED
-8